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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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[REDACTED] ART UNIT

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1644

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172

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Offic Action Summary</b>	<b>Application N .</b>	<b>Applicant(s)</b>
	09/554,567	AGUZZI ET AL.
	<b>Examin r</b>	<b>Art Unit</b>
	Jessica H. Roark	1644

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Peri d f r R pl y

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 25 March 2002.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 35-40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 35-40 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 10 January 2002 is/are: a) accepted or b) objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>15</u> . | 6) <input type="checkbox"/> Other: _____                                    |

## RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/25/02 (Paper No. 16), is acknowledged.  
Claims 29-34 have been cancelled. Claims 1-28 have been cancelled previously.  
Claims 35-40 have been added.  
*Claims 35-40 are pending and are under consideration in the instant application.*
2. This Office Action will be in response to applicant's arguments, filed 3/25/02 (Paper No. 16).  
The rejections of record can be found in the previous Office Action (Paper No. 11).
3. Applicant's cancellation of claims 29-34 has obviated the previous objections and rejections with respect to these claims.  
It is noted that New Grounds of Rejection are set forth herein.
4. Applicant's IDS, filed 3/25/02 (Paper No. 15), is acknowledged.

5. The drawings filed 1/10/02 have been reviewed by the Draftsman and found to fail to comply with 37 CFR 1.84.

Although Applicant has requested in the Response filed 3/25/02 to hold the submission of new formal drawing in abeyance until allowable subject matter has been identified; the Office is no longer holding drawing corrections in abeyance.

The Drawings submitted 1/10/02 have therefore been reviewed in order to provide Applicant with guidance as to the need corrections.

Please see the enclosed form PTO-948.

### INFORMATION ON HOW TO EFFECT DRAWING CHANGES

#### A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

**B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

**Timing of Corrections**

*Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

*The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

7. Claims 35-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: step(s) which result in the “test”; e.g., what reagents are used, which assay system (bioassay, western, IHC, etc.).

Although Applicant has indicated in the response filed 3/25/02 that the instantly pending claims address a similar rejection of record with respect to the canceled claims, instant claims 35-37 still require that a sufficient number of steps be recited that actually results in the “test”.

B) Claims 38-40 are ambiguous in that it is unclear if the “ligand” identifies the particular cell type recited (e.g., anti-CD3 is a “ligand” that identifies T cells), or if the ligand detects the prion.

If the intent is that the ligand detect the prion in the context of an infected B cell, then the claim should clearly indicate that the ligand detects the prion, or that the ligand detects a prion-infected cell but does not detect a non-prion-infected cell (e.g., as described on pages 79 in the last paragraph).

If the ligand is added to identify the B cells and an additional reagent is used to detect the prion, thereby identifying the presence of prions, then the claims should recite an additional method step(s) for detecting the prion, as noted *supra* with respect to claims 35-37.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

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8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

9. Claims 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuroda et al. (Infection and Immunity 1983; 41:154-61, of record, see entire document).

Applicant's arguments, filed 3/25/02, as applied to the instantly pending claims have been fully considered but have not been found convincing.

Applicant argues that Kuroda et al. do not appreciate that infectious agent of CJD is a prion, but rather believe that it is a virus. Applicant argues that because the instant claims recite testing for the presence of or identifying the presence of a prion, that the teachings of Kuroda et al. can not anticipate the instant invention.

However, Kuroda et al. teach that fractionated B cells and T cells obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy (TSE), can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4).

Thus Kuroda et al. teach a method to test for transmissible spongiform encephalopathy comprising obtaining a sample a test sample, collecting B cells and collecting T cells from the sample, and testing the B cells and/or T cells for the presence of transmissible spongiform encephalopathy.

The ability to transmit disease to another animal is a well established means of testing for the presence of an infectious agent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties in the method taught by Kuroda et al.

In particular, although the instant claims now recite that the method tests for the presence of prions associated with transmissible spongiform encephalopathy (claims 35-37), nothing in the claims distinguish the recited method from the method of Kuroda et al. because the instant claims do not require actual detection of the prion per se. The method of Kuroda et al. inherently tests for the presence of prions, even though Kuroda et al. characterized the prion as an unconventional slow acting virus.

It is noted that the CAFC recently held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that when a claimed process is not directed to a new use, *consists of the same steps described in a prior art reference*, and the newly discovered results of the known process *directed to the same purpose* are inherent, the process is not patentable.

The rejection of record is therefore maintained as applied to newly added claims 35-37.

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10. Claims 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Manuelidis et al. (Science 1978; 200:1069-1071, of record, see entire document).

Applicant's arguments, filed 3/25/02, as applied to the instantly pending claims have been fully considered but have not been found convincing.

Applicant argues that Manuelidis et al. do not appreciate that infectious agent of CJD is a prion, but rather believe that it is a virus. Applicant argues that because the instant claims recite testing for the presence of or identifying the presence of a prion, that the teachings of Kuroda et al. can not anticipate the instant invention.

However, Manuelidis et al. teach that maximal infectivity for Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy (TSE), resides in the buffy coat of whole blood, which contains the white blood cells (see entire document, especially the last full paragraph on page 1070).

Since the white blood cells of the buffy coat of whole blood are inherently B cells and T cells, Manuelidis et al. teach a method to test for the presence of transmissible spongiform encephalopathy comprising obtaining a sample of whole blood (which is a heterogeneous mixture of cell types and other components),

collecting B cells and collecting T cells from the sample by isolating the buffy coat,  
and testing the B cells and T cells contained within the buffy coat for the presence of transmissible spongiform encephalopathy.

Manuelidis et al. attribute their ability to demonstrate the infectivity of blood to an increase in the sensitivity of the assay made possible by collecting a specific fraction of whole blood (that inherently containing the B cells and T cells) (see entire document, especially the last full paragraph on page 1070).

The ability to transmit disease to another animal is a well established means of testing for the presence of an infectious agent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties in the method taught by Manuelidis et al.

In particular, although the instant claims now recite that the method tests for the presence of prions associated with transmissible spongiform encephalopathy (claims 35-37), nothing in the claims distinguish the recited method from the method of Manuelidis et al. because the instant claims do not require actual detection of the prion *per se*. The method of Manuelidis et al. inherently tests for the presence of prions, even though Manuelidis et al. characterized the prion as a virus.

It is noted that the CAFC recently held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that when a claimed process is not directed to a new use, *consists of the same steps described in a prior art reference*, and the newly discovered results of the known process *directed to the same purpose* are inherent, the process is not patentable.

The rejection of record is therefore maintained as applied to newly added claims 35-37.

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11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over

O'Rourke et al (US Pat No. 6,165,784, of record),  
and/or Korth et al. (Nature 6 November 1997; 390:74-77, of record),  
in view of

Kuroda et al. (Infection and Immunity 1983; 41:154-61,of record)  
and/or Manuelidis et al. (Science 1978; 200:1069-1071, of record).

Applicant's arguments, filed 3/25/02, as applied to the instantly pending claims have been fully considered but have not been found convincing.

Applicant argues that neither Kuroda et al. nor Manuelidis et al. appreciate that the infectious agent of CJD is a prion, but rather believe that it is a virus. Applicant argues that because the instant claims recite testing for the presence of or identifying the presence of a prion, that the teachings of Kuroda et al. and Manuelidis et al. can not make up for the deficiencies of O'Rourke et al. or Korth et al.

The claims are broadly drawn to methods to test for the presence of prions associated with transmissible spongiform encephalopathy (TSE) in B cells and/or T cells.

O'Rourke et al. teach methods to test for transmissible spongiform encephalopathy in lymphoid tissue using an antibody that serves as a ligand in various immunoassays, including immunohistochemistry, western immunoblots, and dot blots (see entire document, e.g., "Summary of the Invention"). O'Rourke et al. teach that antibody ligands may be either polyclonal sera or monoclonal antibodies (see entire document, e.g., column 5, especially lines 40-50). O'Rourke et al. also teach the importance of developing tests that allow non-invasive preclinical evaluation of animals suspected of being infected with transmissible spongiform encephalopathy, versus the standard approach of assaying brain biopsy material (see entire document, including the "Background of the Invention", especially the summary statement at column 3, lines 27-31). O'Rourke et al. clearly appreciate that prion protein (PrP-Sc) is a major component of infectious material in transmissible spongiform encephalopathy, including the particular forms of transmissible spongiform encephalopathy known as CJD (Creutzfeldt-Jakob disease), BSE and scrapie (reviewed in the Description of the Art at columns 1-3).

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Korth et al. note that prions are the infectious particles that cause transmissible spongiform encephalopathy (see e.g., first line of Abstract), including transmissible spongiform encephalopathy known as CJD (Creutzfeldt-Jakob disease, see e.g., middle of Abstract). Korth et al. teach a method of detecting the prion associated with transmissible spongiform encephalopathy based upon a monoclonal antibody that is specific for the prion form of PrP versus the cellular form of PrP (see entire document, e.g. Abstract). Korth et al. teach that this antibody can be used to identify the prion form of PrP directly, thus providing a basis for a transmissible spongiform encephalopathy test in living humans or animals, by lowering the detection threshold needed (see especially paragraph preceding "Methods" on page 77).

Neither O'Rourke et al. or Korth et al. teach collecting B cells and/or T cells from a test sample and directly testing these cell types for the presence of a prion associated with transmissible spongiform encephalopathy.

Kuroda et al. have been discussed supra and teach that fractionated B cells and T cells obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy, can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4).

Manuelidis et al. have also been discussed supra and teach that maximal infectivity for Creutzfeldt-Jakob disease (CJD), a form of transmissible spongiform encephalopathy, resides in the buffy coat of whole blood, which contains the white blood cells (see entire document, especially the last full paragraph on page 1070). Manuelidis et al. attribute their ability to demonstrate the infectivity of blood to an increase in the sensitivity of the assay made possible by collecting a specific fraction of whole blood (that now known to contain the B cells and T cells) (see entire document, especially the last full paragraph on page 1070).

Thus Kuroda et al. teach that both B cells and T cells can transmit the CJD form of TSE, and Manuelidis et al. teach that it is important to focus on these cellular populations to increase the sensitivity of assays for TSE infectivity. Both O'Rourke et al. and Korth et al. teach that sensitive tests for TSEs are provided by antibody-based assays. And O'Rourke et al. further point out that sampling and testing samples containing lymphocytes is a relatively non-invasive to the animal to be tested. Thus one of ordinary skill in the art at the time the invention was made would have found it obvious to improve the sensitivity of the TSE tests by collecting samples containing B cells and/or T cells and testing for the presence of TSE by using an antibody-based system.

The ordinary artisan at the time the invention was made would have been motivated to test B cells and/or T cells for the presence of TSE using antibodies since this sort of test method utilized a sensitive reagent/ligand, antibodies; to assay cell types that were easily obtainable by non-invasive methods from living animals, in contrast to the other art-recognized approach of brain biopsy. The ordinary artisan at the time the invention was made would have reasonably expected that, as taught by Manuelidis, focusing on a cell type known to be infectious would increase the sensitivity of detection assays, including antibody-based assays. In addition, it was well known in the art at the time the invention was made that once an antibody was developed, the antibody could be used with a reasonable expectation of success to detect an antigen on intact cells, as in a buffy coat of whole blood, or by any of a variety of other assays.

Applicant has argued that because Kuroda et al. and Manuelidis et al. do not appreciate that a prion in the causative agent of Creutzfeldt-Jakob disease in particular and TSEs in general, the ordinary artisan would not have recognized the association between the prion and the B cells and T cells.

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However, clearly one of ordinary skill in the art at the time the invention was made did appreciate that prions were the causative agent of Creutzfeldt-Jakob disease. Therefore, one of ordinary skill in the art at the time the invention was made would have recognized that the earlier studies of Creutzfeldt-Jakob disease, although failing at that time to appreciate the prion component of the disease, nevertheless provided valid data with respect to the association of the causative agent of Creutzfeldt-Jakob disease with B and T cells. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. No claim is allowed.

14. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.  
Patent Examiner  
Technology Center 1600  
July 8, 2002

PHILLIP GAMBEL, PH.D  
PRIMARY EXAMINER  
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7/9/02